

Extension of Time for two (3) months, to and including December 15, 2003 in order to respond, because December 13, 2003 fell on a Saturday.

### REMARKS

By this Office Action, the Examiner has required restriction to one of the following groups of Claims under 35 U.S.C. § 121:

- Group I: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is lipidic, and wherein R1 is lipidic;
- Group II: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is lipidic, and wherein R1 is hydrophilic;
- Group III: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is lipidic, and wherein R1 is amphiphilic;
- Group IV: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is lipidic, and wherein R1 is absent;
- Group V: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is hydrophilic, and wherein R1 is lipidic;
- Group VI: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is hydrophilic, and wherein R1 is hydrophilic;
- Group VII: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is hydrophilic, and wherein R1 is amphiphilic;
- Group VIII: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is hydrophilic, and wherein R1 is absent;
- Group IX: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is amphiphilic, and wherein R1 is lipidic;
- Group X: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is amphiphilic, and wherein R1 is hydrophilic;
- Group XI: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is amphiphilic, and wherein R1 is amphiphilic;

Group XII: Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is amphiphilic, and wherein R1 is absent; and

Groups XIII - Claim(s) 10-11, drawn to methods of using compounds of the general formula  
XXIV CA-Rep-R to manufacture a medicament for treating diseases, wherein groups 13-24 correspond to methods of using compounds of Groups 1-12, respectively.

Initially, the Examiner has asserted that the breadth of the claimed genus of compounds far surpasses that of the family of cationic lipids taught by the instant Specification. Moreover, the Examiner believes that none of the independent Claims recites any requirement that the recited compounds must be lipidic in nature. Furthermore, the Examiner is of the opinion that the Claims are so indefinite as to render it impossible to determine the scope of the claimed subject matter. In support of this opinion, the Examiner has asserted that R1 is defined on page 79 of the instant Application as a group of general formula (III) for which "p" and "q" are integers of "between 0 and 10 inclusive". It is the Examiner's opinion that the phrase "between 0 and 10" clearly means "from 1-9", and that the phrase "0 to 10, inclusively" means "from 0 to 10." However, the Examiner believes the phrase "between 0 and 10 inclusive" is unclear.

Furthermore, the Examiner has asserted that R' is defined at page 82, lines 10-15 as representing either a group of formula NHR6R7, for which R6 and R7 may independently represent a hydrogen atom or an aliphatic radical, with the further limitation that at least one of R6 or R7 must be different from hydrogen and the other must contain between 10 and 22 carbon atoms. Thus, the Examiner believes Claim 1 states that one or both of R6 and R7 may be hydrogen, and also requires that neither R6 nor R7 can be hydrogen.

In light of the alleged ambiguities in the Claims, combined with the vast breadth of the claimed subject matter, the Examiner has asserted that it is difficult to determine what Applicants intend to be the Invention, and the restriction set forth herein is the Examiner's attempt to restrict the Claims fairly.

In response, Applicants respectively disagree with the Examiner and will submit more accurate English translation as a substitute specification that overcomes the Examiner's assertions.

Furthermore, in restricting the Claims as described above, the Examiner has asserted that the Claims of Groups I-XXIV do not relate to a single general inventive concept under PCT Rule 13.1 because, in the Examiner's opinion, under PCT Rule 13.2, they lack the same or corresponding technical features. In order to support this assertion, the Examiner has asserted that the Claims of the instant Application correspond to compositions, methods of making the compositions, and to methods of using the compositions. However, the Examiner believes the compositions first set forth in Claim 1 lack a special technical feature because, in the Examiner's opinion, they are of dissimilar structure and function. The Examiner believes that according to the Administrative Instructions under the PCT, when alternatives of chemical compounds are claimed, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

- (A) all alternatives have a common property or activity, and
- (B) (1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

The Examiner has asserted that in the instant case, not all of the embraced compositions have a common property or activity. For example, the Examiner believes the Claims embrace compositions as set forth in claim 9, which are essentially lipidic in nature, while also allegedly embracing compounds which have no lipidic character at all, i.e. in which 'q' (p. 79, line 14) is 0, and 'R' is NH<sub>2</sub>.

In addition, the Examiner believes the instant Specification does not teach how to use such widely divergent compounds for the same purpose or function, and that no significant structural element is shared by all of the alternatives of the claimed genus. It is the Examiner's opinion that the only structure featured required to be in all of the compounds is a highly generalized heterocycle of from 6 to 9 members in which either of two ring atoms may be either C or N, and in which any of the ring atoms may be substituted with an R1 group that may be hydrophilic, hydrophobic, or amphiphilic. In order to support this position, the Examiner has asserted the Administrative Instructions under the PCT indicate that the heterocyclic rings of variable substitution generally do not have unity of invention absent some teaching of equivalence in the prior art. Thus, the Examiner believes that N atoms, C atoms, hydrophobic substituents, hydrophilic substituents, and amphiphilic substituents clearly lack equivalence in the art of nucleic acid delivery because hydrophobic groups are generally involved in membrane permeabilization whereas hydrophilic groups are generally involved in nucleic acid binding. Moreover, the Examiner believes that N atoms may be positively charged and thereby be

involved in nucleic acid binding, while C atoms generally are not involved in nucleic acid binding.

Finally, the Examiner has asserted that the compounds do not all belong to a recognized class of chemical compounds, as some are lipidic, some are hydrophilic, and some are amphiphilic. Thus, it is the position of the Examiner that none of the criteria (A), (B)(1), or (B)(2) set forth in the Administrative Instructions under the PCT have been met.

In light of the Examiner's beliefs and assertions set forth above, the Examiner contends that the compounds set forth in Claim 1 of the instant Application lack a special technical feature. Thus, it is the Examiner's position that Applicants are not entitled to a grouping of separate categories of Invention, and those methods of making and methods of using a composition of the instant Invention are properly restricted from the compositions themselves.

In response, solely to be responsive to the requirement for restriction, Applicants provisionally elect, WITH TRAVERSAL, to prosecute the invention of Group II, Claims(s) 1-11 and 12-23, drawn to compounds of the general formula CA(R1)-Rep-R, wherein R is lipidic, and wherein R1 is hydrophilic. Furthermore, Applicants respectfully request reconsideration of the requirement for restriction, or in the alternative, modification of the Restriction Requirement to allow prosecution of more than one group of claims designated by the Examiner in the present application, or at least conjoint prosecution of Group II and methods of using compounds of the general formula CA-Rep-R wherein R is lipidic, and wherein R1 is hydrophilic to manufacture a medicament for treating diseases, for reasons provided as follows:

Applicants respectfully submit that the groups of Claims designated by the Examiner fail to

define compositions and methods for using such compositions with properties so distinct as to warrant separate examination and search.

It is respectfully submitted that PCT rule 13.1 states that 'The international application shall relate to one invention only or to a *group of inventions*<sup>1</sup> so linked as to form a single general inventive concept ("requirement of unity of invention") (emphasis added).'

In addition, 37 CFR 1.475(a) specifically state:

(a) An international and national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

In the instant matter, the Examiner has admitted all of the compounds have the general formula CA(R1)-Rep-R. Moreover, as explained on page 3, lines 10-21 of the instant

Application:

...the compounds according to the present invention belong to the family of *cationic lipids and carry a novel cationic region* which confers improved properties on said compounds, in particular reduced cytotoxicity compared with the prior art cationic vectors (emphasis added).

Moreover, the Claims of provisionally elected Group II and well as Group XIV, which is drawn to methods of using the compounds of the Claims of Group II are clearly linked because

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<sup>1</sup> Applicants in no way concede that these groups of Claims are drawn to patentably distinct inventions.

both have a single general inventive concept, i.e., compounds of the general formula CA(R1)-Rep-R, wherein R is lipidic, and wherein R1 is hydrophilic.

In light of the teachings of the instant Specification, it is respectfully submitted that technical relationships exist among all the groups of Claims identified by the Examiner, i.e., they are all cationic vectors, they all are cationic lipids, and they all possess a novel cationic region. Thus, contrary to the Examiner's assertions, these groups of Claims do not lack unity of Invention. In further support of this position, Applicants direct the Examiner to the Box II of the International Search Report for PCT/FR99/00740. No comments are made that the Claims of the instant Application are directed to subject matter that lacks unity of Invention. Furthermore, in making this Requirement, the Examiner has admitted that the Claims of Groups I-XXIV possess common features and utility.

In light of the above, Applicants respectfully submit that the search and examination of the entire Application, or, at least conjoint examination of Groups I-XII is allowable under PCT Rules 13.1 and 13.2 because there is no lack of unity of Invention with respect to all the groups of Claims identified. Accordingly, withdrawal of the Requirement for Restriction, or, at least, modification to permit the conjoint examination of the Claims of Group I-XII is respectfully requested.

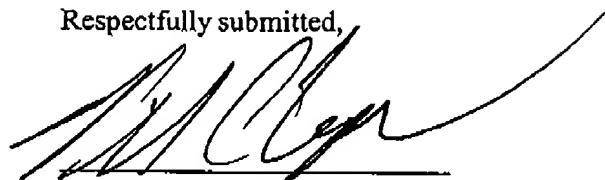
#### *Fees*

No additional fees are believed to be necessitated by the foregoing Response. However, should this be erroneous, authorization is hereby given to charge Deposit Account No. 18-1982 for any underpayment, or credit any overages.

#### CONCLUSION

In view of the above, early action on the merits is courteously solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'W. C. Coppola', written over a horizontal line.

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